REMARKS

Summary of Restriction Requirement

In the Restriction Requirement of February 28, 2008, the Examiner required restriction under 35 U.S.C. 121 and 372 between Group I corresponding to claims 1-5 and 26-36, Group II corresponding to claims 37-46 and Group III corresponding to claims 47-55. The Examiner also required an election of species.

Summary of Amendment

Upon entry of the present Amendment, Claims 1, 29, 37 and 47 will have been amended. Additionally, Claims 2, 30, 38, 49 will have been cancelled. As such, Claims 1, 3-5, 26-29, 31-37, 39-48 and 50-55 remain currently pending.

Applicant's Response

1. **Provisional Election with Traverse**

The Examiner has required restriction under 35 U.S.C. 121 and 372 between the following inventions:

Group I, claims 1-5 and 26-36, drawn to a polysaccharide double-layer microcapsule;

Group II, claims 37-46, drawn to a method for vaccinogenic or therapeutic treatment for the prophylaxis and therapy of infectious or non-infectious diseases; and

Group III, claims 47-55, drawn to a process for the preparation of a polysaccharide double-layer microcapsule.

Applicants provisionally elect, with traverse, the invention of Group I drawn to a polysaccharide double-layer microcapsule. The reasons for the traversal of the restriction requirement are discussed in more detail below.

The Examiner further required election of a single species corresponding to: the absence or presence of hydroxypropylmethylcellulose; a biologically active agent; and the absence or presence of an adjuvant associated with the biologically active substance. The Examiner also

required a listing of all claims readable on the elected species. Accordingly, Applicants hereby elect, with traverse, the species corresponding to: the presence of hydroxypropylmethylcellulose; the presence of a biologically active agent that is lysozyme; and the absence of an adjuvant associated with the biologically active substance. The claims readable on the elected species include claims 1,3-5, 26-29, 32-34, 37, 39-42, 45-48 and 50-53.

2. **Traversal of Restriction Requirement**

The Examiner argues that the inventions listed as Groups I-II above do not relate to a single general inventive concept as required by PCT Rule 13.1, and thus asserts that the claims are subject to requirement for restriction. In particular, the Examiner asserts that polysaccharide double-layer microcapsules are known in the art, and points to the article by Vandenberg et al. as evidence of this fact. The Examiner concludes that the feature cannot constitute a special technical feature as required by PCT Rule 13.2 because it allegedly does not represent a contribution over the prior art. (*See, e.g.,* pages 2-3 of Restriction Requirement). Applicants respectfully traverse this restriction requirement.

In particular, Applicants submit that:

i) no lack of unity objection was raised in the International Preliminary Examination Report issued during the international phase of PCT Application No. PCT/EP2004/051693, to which the present application claims priority;

ii) all the groups of inventions I-III identified by the Examiner are unequivocally directed to a single concept that is polysaccharide double-layer microcapsules for use as carriers for the oral administration of at least one biologically active substance.

Applicants further note that Vandenberg et al. (J. Control Release, 2001) do not disclose or even suggest the polysaccharide double-layer microcapsules of the present invention.

In fact, as clearly discussed in the description of the instant application, the carrier described by Vandenberg et al. is a coacervate formed by alginate and chitosan gelified with calcium chloride solutions entrapping albumin, whereas in the present invention polysaccharide double-layer microcapsules are formed by means of first gelification of alginate solutions

incorporating at least a biologically active substance with a divalent cation in a concentration of 0.5% w/v and then stabilizing a second layer of chitosan with a divalent cation in a concentration of from 10 to 15% w/v, said divalent cation concentration being essential for the formation of said second layer of chitosan. Accordingly, as Vandenberg et al. do not teach the polysaccharide double-layer microcapsules as claimed, the claims are considered to share a special technical feature that makes a contribution over the prior art, and thus the claims have unity under PCT Rule 13.1. The requirement for restriction among Groups I-III is therefore respectfully requested to be withdrawn.

Furthermore, taking into due consideration the mandatory duty to elect one single species, Applicants are submitting herewith an amended claim set wherein the polymer hydroxypropylmethylcellulose (HPMC) is dispersed in the alginate solutions.

Therefore, the current amended claim 1 recites "Polysaccharide double-layer microcapsules constituted by an outer layer of chitosan and an inner layer of alginate wherein they are obtained:

- from solutions of alginate with initial concentrations ranging from 2 to 4% w/v comprising the further polymer hydroxypropylmethylcellulose at the initial concentration of 0.4% w/v;
- from solutions of chitosan with initial concentrations ranging from 0.1 to 0.5% w/v;
- from solutions of divalent ions with concentrations of 0.5% w/v, when the divalent ion functions as a gelification agent of the alginate to form single-layer capsules of alginate encapsulating at least one biologically active substance, and ranging from 10 to 15% w/v when the divalent ion has a stabilizing function of the double layer capsules for use as carriers for the oral administration of said biologically active substances."

The same amendment has also been made to claims 29, 37 and 47. Applicants respectfully submit that no new matter has been added by the current amendment, as the subject matter added corresponds to that recited in original claims 2, 30, 38 and 49, which claims are being canceled herewith.

As such, Applicants respectfully submit that the claims, as currently amended, are directed to a single invention and that the restriction requirement is no longer proper. Accordingly, the restriction requirement is traversed, and Applicants respectfully request that the requirement for restriction be withdrawn.

If any additional fee is required, please charge Deposit Account Number 19-4330.

Respectfully submitted,

Date: May 20, 2008 By: 

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